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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/801,986	03/16/2004	Leonard D. Kohn	IMT 2-001	3062

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/801,986	KOHN ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/30/06;8/28/06;2/9/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-107* is/are pending in the application.

4a) Of the above claim(s) *56 and 69-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54, 55, 57-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-28-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A Preliminary Amendment filed May 30, 2006 is acknowledged. Claims 1-53 are canceled. New claims 54-107 are presented and represent all of the claims under initial consideration.

Applicants' Response filed August 28, 2006 to the Restriction Requirement and Response filed February 9, 2007 to the Election of species Requirement are acknowledged.

Applicants have elected with traverse Group I, drawn to methods for inhibiting cell adhesion, optionally wherein the cell adhesion is VCAM-1 mediated, claims 54, 55, 57-95 and 97. The traversal is on the grounds that, in Applicants' view, all of the claims relate to cell adhesion and to certain compounds that are effective in inhibiting cell adhesion.

In response to the Election of Species Requirement, Applicants elected 5-methyl methimazole, **1-methyl-5-phenyl-imidazoline–2(3) thione**.

Applicants' argument has been given due consideration but is not found persuasive. A complete search for all those conditions and pathologies wherein cell adhesion is a fundamental characteristic is a substantial undertaking. Such a search is drawn to an unduly broad amount of subject matter. Any pathology wherein body tissues that are normally separate but now grow together is encompassed. As such, an undue burden is presented to the Examiner.

Accordingly, the Restriction Requirement as set forth July 27, 2006 is deemed proper and is adhered to. The Restriction Requirement is hereby made FINAL.

Claims 56 and 69-107, are presently withdrawn from consideration by the Examiner, as drawn to non-elected subject matter, 37 CFR 1.142(b). Claims 54, 55 and 57-68, drawn to methods for inhibiting cell adhesion, optionally wherein the cell adhesion is VCAM-1 mediated, comprising administering 5-methyl methimazole, represent the subject matter initially under consideration. Re-affirmation of the elections is requested when Applicants respond to this Office Action.

An Information Disclosure Statement filed August 28, 2006 is further acknowledged and has been reviewed.

Claim 57 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Parenthetical subject matter renders the claim in which it appears as indefinite. It is unclear whether or not a claim limitation is intended.

Claim 57 recites the limitation "the disease or condition". There is insufficient antecedent basis for this limitation in the claim.

Claim 57 depends from independent claim 54, which fails to recite a "disease or condition."

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 54, 55 and 57-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 59-67 of copending Application No. 10/912948. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to the administration of methimazole derivatives and/or cyclic thione derivatives, which encompass 5-methyl methimazole, for use in the treatment of inflammatory bowel disease such as Crohn's disease and ulcerative colitis.

Claims 54, 55 and 57-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 139-304 of copending Application No. 11/130922. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to the administration of methimazole derivatives and/or cyclic thione derivatives, which encompass 5-methyl methimazole, for use in the treatment of various autoimmune/inflammatory diseases that encompass those presently claimed.

Claims 54, 55 and 57-68 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 61-64 of

copending Application No. 10/830898. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application are drawn to the administration of methimazole derivatives and/or cyclic thione derivatives, which encompass 5-methyl methimazole, for use in the treatment of various autoimmune diseases, disorders, conditions or symptoms that encompass those presently claimed.

These are provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 54, 55 and 57-68 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-33 and 42-44 of U.S. Patent No. 6,365,616. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patent are drawn to administration of methimazole derivatives and/or cyclic thione derivatives, which clearly encompass 5-methyl methimazole, for use in the treatment of autoimmune diseases, as for example Graves' disease.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 54, 55 and 57-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohn et al., U.S. Patent 6,365,616.

Kohn teaches the administration of 5-methyl methimazole to treat autoimmune diseases such as autoimmune glomerulonephritis (instant claim 57) or systemic lupus erythromatosus (instant claim 68). See column 13 where a particularly preferred subset of methimazole derivatives is described at line 30 where X = S, Y, R^2 in the 3-position, R^1 and R^4 = H and R^2 in the 1-position is methyl. Further, see Table 15, column 49, where 5-methylmethimazole is, *inter alia*, specifically disclosed.

The inhibition or suppression of cell adhesion, optionally VCAM-1 and/or E-selectin mediated, as well as inhibition or suppression of cytokine-induced cell adhesion, optionally wherein the cytokine is TNF-alpha, are inherent mechanisms of action following the administration of 5-methyl methimazole.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54, 55 and 57-68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 54, 55, 58 and 61 recite "derivatives," with respect to various tautomeric and non-tautomeric methimazole compounds. There is insufficient written description for this claim limitation in the disclosure.

> M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

The term "derivative" encompasses a plethora of possible compounds. For example, any carbon-containing compound could, in the broadest interpretation, be a "derivative" of the claimed chemical structure. Further, the structural features of all "derivatives" of the recited tautomeric and non-tautomeric methimazole compounds have not been defined. No description of any methods of synthesizing such broad subgenera of compounds is disclosed.

Accordingly, it is not clear Applicant was in possession of the full scope of the claimed compounds at the time the invention was made. Adequate description requires more than a mere statement that derivatives are part of the invention. The skilled artisan could not "immediately envisage" the claimed compounds based on the description provided in the disclosure.

Applicants may consider adding those compounds contemplated that are disclosed in the specification as tautomeric and non-tautomeric methimazole compounds to the independent claims.

Claims 58-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to preventing cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse diseases selected from the group consisting of adult respiratory distress syndrome, AIDS, allergy conditions, arteriosclerosis, arthritis, asthma, atherosclerosis, cardiovascular diseases, detaching retina, harmful platelet aggregation, inflammation, inflammatory bowel diseases, multiple sclerosis, neoplastic diseases, ophthalmic inflammatory conditions, osteoarthritis, osteoporosis, psoriasis, regional enteritis, rejection after transplantation, reocclusion following thrombolysis, reperfusion injury, Sjogren's Syndrome, skin inflammatory diseases, systemic lupus erythematosus, thrombosis, Type I diabetes, thyroiditis and wounds.

The specification does not reasonably provide enablement for the methods of prevention within the full scope of the claimed compounds.

Further, claim 57 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547, the court recited eight factors to consider when assessing whether or not a disclosure would require undue experimentation. These factors are:

1) the quantity of experimentation necessary

2) the amount of direction or guidance provided

3) the presence or absence of working examples

4) the nature of the invention

5) the state of the art

6) the relative skill of those in the art

7) the predictability of the art and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The invention is drawn to preventing cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse autoimmune and/or inflammatory diseases.

Such characterization encompasses, in addition to numerous disease states of unrelated organ systems, inherent molecular mechanisms of action.

Claim 57 is drawn to a diverse group of diseases or conditions of unrelated etiology.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. with expertise in the area of immunology.

However, that factor is outweighed by the unpredictable nature of cell adhesion, optionally mediated by VCAM-1 or E-selectin or the cytokine TNF-alpha. Calvey et al., J. Invest. Surgery (abstract), is cited for evidentiary purposes only, to show the complexity of cell adhesion inhibition.

The instant specification provides no support for the treatment or prevention of any specific disease state following the administration of 5-methyl methimazole. The disclosure is clearly not predictable for prevention of any specific disease state or preventing cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse autoimmune and/or inflammatory diseases.

The skilled artisan would not reasonably expect that 5-methyl methimazole could be used to prevent any occurrence – under any circumstance - of any of the recited disease states, or to prevent cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse autoimmune and/or inflammatory diseases.

The breadth of the claims

The claims are extremely broad and inclusive of factors of diverse etiology comprising administering 5-methyl methimazole.

The amount of direction or guidance provided and the presence or absence of working examples

There are no working examples drawn to a prevention modality in which 5-methyl methimazole is shown to be clinically effective for inhibiting cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse autoimmune and/or inflammatory diseases.

No guidance is provided drawn specifically to methods of prevention. Such an assertion is clearly beyond the scope of the instantly claimed invention. The term "prevention" is an absolute definition that means to stop from occurring and thus requires a higher standard for enablement than does "therapeutic" or "treat". It is well established in the medical arts that the vast majority of diseases suffered by mankind cannot be totally prevented with current therapies.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to dosages and dosing regimens as they are contemplated for the plethora of disease states that is encompassed in the claim language. The skilled artisan would expect methods of prevention to be very specific and highly unpredictable absent a clear understanding of the biochemical basis for 5-methyl methimazole. The instant specification sets forth no such understanding. No direction is provided to distinguish therapy among the numerous pathologies herein claimed. Absent reasonable *a priori* expectations of success for using a particular inhibitor to prevent cell adhesion or cytokine-induced cell adhesion, one skilled in the immunology art would have to test extensively numerous laboratory models of diseases using various dosages and dosing regimens to discover which is effective. Since each prospective embodiment, as well as future embodiments as the art progresses, would have to be empirically tested, undue experimentation would be required to practice the invention as it is claimed in its current scope. The specification provides inadequate guidance to do otherwise.

Prevention entails the complete and absolute inhibition of the onset of nocturnal acid breakthrough and any manifestation of the disease entirely.

Due to the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that cell adhesion, cytokine-induced cell adhesion, cytokine-induced cell adhesion-associated inflammation, cell adhesion associated with immune or autoimmune responses and diverse autoimmune and/or inflammatory diseases could be prevented following the administration of 5-methyl methimazole. Accordingly, the instant claims do not comply with the enablement requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phyllis Spivack

May 13, 2007

Phyllis G. Spivack

1614 PHYLLIS SPIVACK
PRIMARY EXAMINER